

Claims

1. One or more isolated nucleic acid sequences selected from the group consisting of those sequences identified in Figure 6A which correspond to genes 1-5807 identified in Figure 6 and/or those sequences identified in Figure 13.
- 5 2. A vector comprising an isolated nucleic acid sequence of claim 1.
3. A host cell comprising the vector of claim 2.
4. A composition comprising one or more chondrocyte enriched or chondrocyte-specific nucleic acid sequences isolated from one or more sources selected from the group consisting of (a) fetus, (b) normal, (c) mild osteoarthritic, (d) moderate osteoarthritic,
10 (e) marked osteoarthritic and (f) severe osteoarthritic cartilage samples.
5. A composition comprising one or more nucleic acid sequences selected from the group consisting of sequences identified in Figure 6B whose sequences are disclosed in Figure 14.
- 15 6. A composition comprising one or more nucleic acid sequences selected from the group consisting of sequences identified in Figure 6C whose sequences are disclosed in Figure 14.
7. A composition comprising one or more nucleic acid sequences selected from the group consisting of sequences identified in Figure 6D whose sequences are disclosed in Figure 14.
- 20 8. A composition comprising one or more nucleic acid sequences selected from the group consisting of those sequences identified in Figure 6E whose sequences are disclosed in Figure 14.

9. A composition comprising one or more nucleic acid sequences selected from the group consisting of those sequences identified in Figure 6B, 6C, 6D, and 6E whose sequences are disclosed in Figure 14.

10. A composition comprising one or more nucleic acid sequences wherein at least one of said nucleic acid sequences is differentially expressed in cartilage from a patient diagnosed with mild osteoarthritis relative to cartilage from a normal individual, wherein cartilage isolated from said normal individual is isolated from cartilage tissue obtained less than 14 hours post-mortem.

11. A composition comprising one or more nucleic acid sequences wherein at least one of said nucleic acid sequences is differentially expressed in cartilage from a patient diagnosed with severe osteoarthritis relative to cartilage derived from a normal individual, wherein cartilage isolated from said normal individual is isolated from cartilage tissue obtained less than 14 hours post-mortem.

12. A composition comprising one or more nucleic acid sequences wherein at least one of said nucleic acid sequences is differentially expressed in cartilage from a patient diagnosed with marked osteoarthritis relative to cartilage derived from a normal individual, wherein cartilage isolated from said normal individual is isolated from cartilage tissue obtained less than 14 hours post-mortem.

13. A composition comprising one or more nucleic acid sequences wherein at least one of said nucleic acid sequences is differentially expressed in cartilage from a patient diagnosed with moderate osteoarthritis relative to cartilage derived from a normal individual, wherein cartilage isolated from said normal individual is isolated from cartilage tissue obtained less than 14 hours post-mortem.

14. A composition comprising one or more nucleic acid sequences wherein at least one of said nucleic acid sequences is differentially expressed in cartilage from a patient diagnosed with mild osteoarthritis relative to cartilage isolated from a fetus.

15. A composition comprising one or more nucleic acid sequences wherein at least one of said nucleic acid sequences is differentially expressed in cartilage from a patient diagnosed with moderate osteoarthritis relative to cartilage isolated from a fetus.
- 5 16. A composition comprising one or more nucleic acid sequences wherein at least one of said nucleic acid sequences is differentially expressed in cartilage from a patient diagnosed with marked osteoarthritis relative to cartilage isolated from a fetus.
17. A composition comprising one or more nucleic acid sequences wherein at least one of said nucleic acid sequences is differentially expressed in cartilage from a patient diagnosed with severe osteoarthritis relative to cartilage isolated from a fetus.
- 10 18. A composition comprising one or more nucleic acid sequences wherein at least one of said nucleic acid sequences is differentially expressed in cartilage from normal individual relative to cartilage isolated from a fetus.
- 15 19. A composition comprising one or more nucleic acid sequences wherein at least one of said nucleic acid sequences is differentially expressed in cartilage isolated from any two or more of the following sources: (a) fetus (b) patient with mild osteoarthritis, (c) patient with moderate osteoarthritis, (d) patient with marked osteoarthritis, (e) patient with severe osteoarthritis and (f) cartilage isolated from a normal individual isolated from cartilage tissue obtained less than 14 hours post-mortem.
- 20 20. A composition comprising one or more nucleic acid sequences identified in Figure 9 and/or sequences identified in Figure 6A which correspond to the genes disclosed in Figure 9.
21. A composition comprising one or more nucleic acid sequences identified in Figure 11 and/or sequences identified in Figure 6A which correspond to the genes disclosed in Figure 11.

22. A composition comprising one or more nucleic acid sequences identified in Figure 6A which correspond to the genes disclosed in Figure 15 and Figure 16.

23. A composition comprising one or more nucleic acids sequences identified in Figure 6A which correspond to the genes disclosed in Figure 6.

5 24. A composition comprising one or more nucleic acid sequences comprising one or more of the sequences disclosed in Figure 13.

25. An array comprising:

10 a plurality of nucleic acid members and a solid substrate, wherein at least one member is differentially expressed in cartilage from a patient diagnosed with mild osteoarthritis as compared to cartilage from a normal individual, and wherein each nucleic acid member has a unique position on said array and is stably associated with said solid substrate.

26. An array comprising:

15 a plurality of nucleic acid members and a solid substrate, wherein at least one member is differentially expressed in cartilage isolated from a patient diagnosed with severe osteoarthritis as compared to cartilage from a normal individual, and wherein each nucleic acid member has a unique position on said array and is stably associated with said solid substrate.

27. An array comprising:

20 a plurality of nucleic acid members and a solid substrate, wherein at least one member is differentially expressed in cartilage isolated from a patient diagnosed with moderate osteoarthritis as compared to cartilage from a normal individual, and wherein each nucleic acid member has a unique position on said array and is stably associated with said solid substrate.

28. An array comprising:

a plurality of nucleic acid members and a solid substrate, wherein at least one member is differentially expressed in cartilage isolated from a patient diagnosed with marked osteoarthritis as compared to cartilage from a normal individual, and wherein each nucleic acid member has a unique position on said array and is stably associated with said solid substrate.

29. An array comprising:

a plurality of nucleic acid members and a solid support, wherein at least one member is differentially expressed in cartilage isolated from a fetus as compared to cartilage from a normal individual, and wherein each nucleic acid member has a unique position on said array and is stably associated with said solid substrate.

30. An array comprising:

a plurality of nucleic acid members and a solid substrate, wherein at least one member is differentially expressed in cartilage isolated from any two or more of the following sources: (a) fetus, (b) patient with mild osteoarthritis (c) patient with moderate osteoarthritis (d) patient with marked osteoarthritis (e) severe osteoarthritis, and (f) cartilage from a normal individual, and wherein each nucleic acid member has a unique position on said array and is stably associated with said solid substrate.

31. The array of claim 25, 26, 27, 28 29 or 30 wherein said normal individual is living.

32. The array of claim 25, 26, 27, 28, 29 or 30 wherein said cartilage isolated from said normal individual is isolated from cartilage tissue less than 14 hours post-mortem.

33. The array of claim 25, 26, 27, 28, 29, 30 wherein each nucleic acid member is at least 50 nucleotides.

34. The array of claim 25, 26, 27, 28, 29, 30 wherein said array comprises from 10 to 20,000 positions.
35. The array of claim 25, 26, 27, 28, 29, 30 further including negative and positive control sequences and RNA quality control sequences selected from the group consisting of: cDNA sequences encoded by housekeeping genes, plant gene sequences, bacterial sequences, PCR products and vector sequences.
36. A method of diagnosing mild osteoarthritis in a patient, comprising: hybridizing a nucleic acid sample corresponding to RNA to an array comprising a solid substrate and a plurality of nucleic acid members, wherein at least one member is differentially expressed in cartilage isolated from a patient diagnosed with mild osteoarthritis, as compared to cartilage isolated from a normal individual, wherein cartilage isolated from said normal individual is isolated from cartilage tissue less than 14 hours post-mortem, and wherein each nucleic acid member has a unique position and is stably associated with the solid substrate, and wherein hybridization of said nucleic acid sample to one or more said differentially expressed nucleic acid members is indicative of mild osteoarthritis.
37. A method of diagnosing moderate osteoarthritis in a patient comprising: hybridizing a nucleic acid sample corresponding to RNA to an array comprising a solid substrate and a plurality of nucleic acid members, wherein at least one member is differentially expressed in cartilage isolated from a patient diagnosed with moderate osteoarthritis, as compared to cartilage isolated from a normal individual, wherein cartilage isolated from said normal individual is isolated from cartilage tissue less than 14 hours post-mortem, and wherein each nucleic acid member has a unique position and is stably associated with said solid substrate, and wherein hybridization of said nucleic acid sample to one or more said differentially expressed nucleic acid members is indicative of moderate osteoarthritis.

38. A method of diagnosing marked osteoarthritis in a patient comprising: hybridizing a nucleic acid sample corresponding to RNA to an array comprising a solid substrate and a plurality of nucleic acid members, wherein at least one member is differentially expressed in cartilage isolated from a patient diagnosed with marked osteoarthritis, as compared to cartilage isolated from a normal individual, wherein cartilage isolated from said normal individual is isolated from cartilage tissue less than 14 hours post-mortem, wherein each nucleic acid member has a unique position and is stably associated with said solid substrate, and wherein hybridization of said nucleic acid sample to one or more said differentially expressed nucleic acid members is indicative of marked osteoarthritis.

39. A method of diagnosing severe osteoarthritis in a patient comprising: hybridizing a nucleic acid sample corresponding to RNA to an array comprising a solid substrate and a plurality of nucleic acid members, wherein at least one member is differentially expressed in cartilage isolated from a patient diagnosed with severe osteoarthritis, as compared to cartilage isolated from a normal individual, wherein cartilage isolated from said normal individual is isolated from cartilage tissue less than 14 hours post-mortem, wherein each nucleic acid member has a unique position and is stably associated with the solid substrate, and wherein hybridization of said nucleic acid sample to one or more said differentially expressed nucleic acid members is indicative of severe osteoarthritis.

40. The method of claim 36, 37, 38 or 39 further comprising the step of isolating RNA from said patient.

41. The method of claim 40 further comprising the step of isolating RNA from a cartilage sample.

42. The method of claim 40 further comprising the step of isolating RNA from a blood sample.

43. The method of claim 40 further comprising the step of isolating RNA from a synovial fluid sample.
44. The method of claim 36, 37, 38, or 39 further comprising the step of preparing a nucleic acid sample corresponding to the said RNA.

- 5 45. A method of identifying an agent that increases or decreases the expression of a nucleic acid sequence that is differentially expressed in a chondrocyte derived from any two or more of the following chondrocyte disease or developmental stages: fetal, mild osteoarthritic, moderate osteoarthritic, marked osteoarthritic and severe osteoarthritic, comprising:

10 incubating a chondrocyte derived from a normal individual with a candidate agent, wherein said chondrocyte is isolated from a cartilage sample obtained from said normal individual less than 14 hours post-mortem; isolating RNA from said chondrocyte; and hybridizing a probe to said RNA, said probe corresponding to a nucleic acid sequence which is differentially expressed in a
15 chondrocyte derived from any two or more sources selected from the group consisting of: fetal, normal, mild osteoarthritic, moderate osteoarthritic, marked osteoarthritic and severe osteoarthritic, wherein differential hybridization of said probe to said RNA from said normal individual relative to RNA from one or more of fetal, mild osteoarthritic, marked osteoarthritis
20 moderate osteoarthritis or severe osteoarthritic samples is indicative of the level of expression of RNA corresponding to a differentially expressed chondrocyte-specific nucleic acid sequence, and wherein, as a result of said incubation step in the presence of said candidate agent, a change in the level of expression of said nucleic acid sequence is indicative of an agent that increases
25 or decreases the expression of said chondrocyte specific nucleic acid sequence.

46. A method of preparing a chondrocyte cDNA library comprising,

a)isolating chondrocytes from a cartilage sample derived from one or more normal individuals, wherein said cartilage sample is obtained less than 14 hours post-mortem;

b) isolating mRNA from said chondrocytes;

c) synthesizing cDNA from said mRNA; and

d) ligating said cDNA into a vector.

47. A method of preparing a chondrocyte cDNA library comprising,

a) isolating chondrocytes from a cartilage sample derived from one or more living normal individuals;

b) isolating mRNA from said chondrocytes;

c) synthesizing cDNA from said mRNA; and

d) ligating said cDNA into a vector.

48. A method of preparing a chondrocyte cDNA library comprising,

a) isolating chondrocytes from a cartilage sample derived from one or more patients diagnosed with mild osteoarthritis

b) isolating mRNA from said chondrocytes;

c) synthesizing cDNA from said mRNA; and

d) ligating said cDNA into a vector.

49. A method of preparing a chondrocyte cDNA library comprising,

a) isolating chondrocytes from a cartilage sample derived from one or more patients diagnosed with moderate osteoarthritis

- b) isolating mRNA from said chondrocytes;
- c) synthesizing cDNA from said mRNA; and
- e) ligating said cDNA into a vector.

50. A method of preparing a chondrocyte cDNA library comprising,

- 5 a) isolating chondrocytes from a cartilage sample derived from one or more patients diagnosed with marked osteoarthritis
- b) isolating mRNA from said chondrocytes;
- c) synthesizing cDNA from said mRNA; and
- d) ligating said cDNA into a vector.

51. A method of preparing a chondrocyte cDNA library comprising,

- a) isolating chondrocytes from a cartilage sample derived from one or more patients diagnosed with severe osteoarthritis
- b) isolating mRNA from said chondrocytes;
- c) synthesizing cDNA from said mRNA; and
- 15 f) ligating said cDNA into a vector.

52. A method of preparing a chondrocyte cDNA library comprising,

- a) isolating chondrocytes from one or more fetuses;
- b) isolating mRNA from said chondrocytes;
- c) synthesizing cDNA from said mRNA; and
- 20 d) ligating said cDNA into a vector.

53. A method of making an array comprising a plurality of nucleic acid members selected from those sequences identified in Figure 14 on a solid support, said support comprising a surface with a plurality of pre-selected unique regions, said method comprising:

5 spotting each nucleic acid member individually onto a unique pre-selected region and stably attaching each nucleic acid member to said solid support.

54. The method of claim 53, wherein at least one nucleic acid member is differentially expressed in cartilage isolated from two or more sources selected from the group consisting of: (a) a fetus or a patient diagnosed with (b) mild, (c) moderate, (d) marked, (e) severe osteoarthritis, and (f) cartilage isolated from a normal individual.

55. The method of claim 54, wherein the cartilage isolated from one or more normal individuals is isolated from cartilage tissue less than 14 hours post-mortem.

56. A method of claim 54 wherein the cartilage is isolated from one or more living normal individuals.

57. A kit comprising an array of claim 25, 26, 27, 28, 29, 30 and packaging means therefore.